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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 05/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/624,289	CIRILLO ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-22 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, 8-17, drawn to the compounds of formula II where G is all carbocyclic claimed, Ar is all carbocyclic rings claimed, X is all carbocyclic rings claimed, Y is as claimed, R1 is as claimed except the heterocyclic or heteroaryl rings claimed, R2, R4, R5 is as claimed, R3 is as a carbocyclic ring, R6 is as claimed, R7-R10, R12, R13-R15, R17, R19, R25, R26, are the carbocyclic rings claimed, R11 and R16 are as claimed, R18 is as claimed, R20 is C1-10 alkyl optionally partially or fully hydrogenated,or phenyl, R21 is as claimed, R22, R23, R24 can be any of the radicals claimed except pyridinyl, R23 and R24 can not come together to form a heterocyclic ring, m is as claimed, W is O or S, pharmaceutical compositions, classified in class 564, subclass 306.

II. Claims 1-5, 8-17, drawn to the compounds of formula II where G is pyridinyl, pyridonyl, quinolinyl, dihydroquinolinyl, Ar is quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, X is pyridinyl, Y is as claimed, Z is pyridinyl-C1-3 alkyl, R1 is pyridinyl, R2, R4, R5 is as claimed, R3 is are the rings claimed that are 6 membered rings saturated or unsaturated with 1 N and 5 carbon atoms, R6 is as claimed, R7-R10, R12-R15, R17, R19, R25, R26 are piperidinyl or pyridinyl, R11 and R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed,

R22, R23, R24 are pyridinyl, R23 and R24 do not come together to form a heterocyclic or heteroaryl ring, m is as claimed, W is O or S , pharmaceutical compositions, classified in class 546, subclass 155.

III. Claims 1-2, 3, 8-17, drawn to the compounds of formula II where G is pyrimidinyl, pyridazinyl, pyrazinyl, piperazinyl , tetrahydropyridinyl, homopiperidinyl, Ar is benzofuranyl, dihydrobenzofuranyl, benzothienyl, dihydrobenzylthienyl, X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 544, subclass 238.

IV. Claims 1, 8-17, drawn to the compounds of formula II where G is benzimidazolyl, imidazolinyl, Ar is benzofuranyl, dihydrobenzofuranyl, benzothienyl, dihydrobenzylthienyl, X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are

as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 548, subclass 467.

V. Claims1, 8-17, drawn to the compounds of formula II wherein G is benzoxazolyl, benzoxazolonyl, Ar is benzofuranyl, dihydrobenzofuranyl, benzothienyl, dihydrobenzylthienyl, X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 549, subclass 57.

VI. Claims 1, 8-17, drawn to the compounds of formula II wherein G is dioxanyl, dithianyl, benzodioxolyl, benzo [1,3]dioxol-2-only, Ar is benzofuranyl, dihydrobenzofuranyl, benzothienyl, dihydrobenzylthienyl, X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-

C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 549, subclass 57.

VII. Claims 1, 8-17, drawn to the compounds of formula II where G is tetrahydrofuranyl, tetrahydrothiophenyl, thioxanyl, benzothiophenyl, Ar is benzofuranyl, dihydrobenzofuranyl, benzothienyl, dihydrobenzylthienyl, X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 549, subclass 57.

VIII. Claims 1, 2, 4, 8-17, drawn to the compounds of formula II wherein G is equal to indolyl, indolinyl, indolonyl, indolinonyl, phthalimidyl, pyrrolinyl, Ar is benzofuranyl, dihydrobenzofuranyl, benzothienyl, dihydrobenzylthienyl,

X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 548, subclass 455.

IX. Claims 1, 8-17, drawn to the compounds of formula II wherein G is oxetanyl, Ar is as claimed, X is any ring claimed that is a 5 membered heterocyclic or heteroaryl ring containing 1 O or S and 5 carbons, Y is as claimed, Z is tetrahydrofuranyl-C1-3 alkyl, each R1 is any ring claimed that is a 5 membered heterocyclic ring or heteroaryl ring with 1 O or S and 5 carbons, R2, R3, R5, R6 are as claimed, R25 and R26 are as claimed, R11, R16 are as claimed, R18 is as claimed, R20 is as claimed, R21 is as claimed, R22, R23, R24 are as claimed except that R23 and R24 can not come together to form a heterocyclic ring, m is 0, 1, or 2, W is O or S, pharmaceutical compositions, classified in class 549, subclass 57.

X. Claims 1, 8-17, drawn to the compounds of formula II wherein G is morpholinyl, thiomorpholinyl, Ar is as claimed, X, Y, W, Z are as claimed,

R1, R2, R3, R4, R5, R7, R6, R20-R26, m, are as claimed, classified in class 549, subclass 57.

XI. Claims 1, 8-17, drawn to the compounds of formula II wherein G is tetrahydropyranyl, dihydropyranyl, Ar is carbocyclic ring, and X, Y, W, Z are as claimed, R1, R2, R3, R4, R5, R7, R6, R20-R26, m are as claimed, pharmaceutical compositions, classified in class 549, subclass 416.

XII. Claims 1, 8-17, drawn to the compounds of formula II wherein G is tetramethylene sulfonyl, tetramethylene sulfoxide, Ar is as claimed, X, Y, W, Z are as claimed, R1, R2, R3, R4, R5, R7, R6, R20-R26, m, pharmaceutical compositions, are as claimed, classified in class 549, subclass 57.

XIII. Claims 1, 8-17, drawn to the compounds of formula II wherein G is oxazolinyl, benzoxazolyl, benzooxaolonyl, benzo [1,4]oxazin-3-only, oxazolinyl, thiazolinyl, dihydroxazinyl, thiazoldinyl, Ar is any ring claimed that is a carbocyclic aryl ring, X, Y, W, Z are as claimed, R1, R2, R3, R4, R5, R7, R6, R20-R26, m, are as claimed, pharmaceutical compositions, classified in class 549, subclass 57.

XIV. Claims 1, 8-17, drawn to the compounds of formula II wherein G is heptacanyl, Ar is isoqinolinyl, tetrahydro quinolinyl, tetrahydroisoquinolinyl, , X, Y, W, Z are as claimed, R1, R2, R3, R4, R5, R7, R6, R20-R26, m, pharmaceutical compositions, are as claimed classified in class 546, subclass 15.

XV. Claims 18-19, drawn to the method of treating a disease mediated by cytokines, and the various cytokine-mediated diseases with a compound of claim 1, classified in class 514, subclass 252.04.

XVI. Claim 20, drawn to drawn to the method of treating the various diseases with a compound of claim, classified in class 514, subclass 252.04.

XVII. Claim 21, 22 drawn to a method of making a compound of formula II or formula III, classified in class 546, subclass 155.

If Group XV or XVI is elected, then election of one of the following methods of use is required:

A. Method of treating rheumatoid arthritis

B. Method of treating osteoarthritis

C. Method of treating Crohn's disease

D. Method of treating ulcerative colitis

E. Method of treating multiple sclerosis

F. Method of treating Guillain-Barre syndrome

G. Method of treating psoriasis

H. Method of treating graft versus host disease

I. Method of treating systemic lupus erythematosus

J. Method of treating diabetes

K. Method of treating toxic shock syndrome

L. Method of treating osteoporosis

M. Method of treating Alzheimer's disease

N. Method of treating acute and chronic pain

O. Method of treating contact dermatitis

P. Method of treating atherosclerosis

Q. Method of treating myocardial infarction

R. Method of treating thermal injury

S. Method of treating adult respiratory distress syndrome (ARDS)

T. Method of treating multiple organ injury secondary to trauma

U. Method of treating acute glomerulonephritis

V. Method of treating dermatoses with acute inflammatory components

W. Method of treating acute purulent meningitis

X. Method of treating hemodialysis

Y. Method of treating leukopherisis

Z. Method of treating granulocyte transfusion associated syndromes and Necrotizing entrerocolitis

In accordance with the decisions in ***In re Harnisch***, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and ***Ex parte Hozumi***, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious

under 35 U.S.C. 103.

Where an election of any one of Groups I-XVII is made, an election of a single compound (or set of compounds) is further required including an exact definition of each substitution on the base molecule of formula I, wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has a substituent group R1, wherein R1 is recited to be any one of H, OH, COOH, aryl, alkoxy, halogen, amino, etc., then applicant must select a single substituent of R1, for example OH or aryl, and each subsequent variable position. In the instant case, upon election of a single compound (or set of compounds), the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim which fall into the same class and subclass as the elected compound (or set of compounds), but may also include additional compounds which fall in related subclasses. Examination will then proceed on the elected compound AND the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits. Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds along with process of using said compound under examination. This will be set forth by reference to specific class(es) and subclass(es) examined. Should applicant traverse on the

ground that the compounds are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventors must be amended in compliance with 37C.F.R. 1.48(b) if one of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37CFR 1.17(i).

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can **set forth** a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise

caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:

Groups XV-XVI and are distinct and independent from Group XVII because they are directed to different statutory classes of invention and, the practice of one of Inventions XV-XVI would not result in the practice of the other Invention, i.e., treating osteoporis is not a process that prepares *per se* the compounds.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

The inventions are distinct, each from the other because of the following reasons:

In the instant case the different inventions have achieved a separate status in the art, have separate fields that aren't coextensive, and are capable of supporting separate patents. Further, a prior art reference that would anticipate the claims under 35 USC 102(b) would not render obvious the same claim(s) under 35 U. S. C. 103 (a) with respect to another member. Searching the entire genus would be a burden on the USPTO in terms of time and expense. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art

because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons: Groups I-XIV and XVII are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product can be made by another material different process (MPEP 806.05(f)). In the instant case, the product as claimed can be made by another materially process as demonstrated by in Qui et. al., (See Reference U, page 1552) and in US Patent 6180675, which are directed to two different processes of preparing compounds of formula (I).

Groups I-XIV and XV and XVI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (MPEP 806.05(h)). In the instant case, the product as claimed can be used in a materially different process of using that product as demonstrated throughout the specification and in claims 18, 19, and 20 which are directed to several different methods of using the product, for example treating Crohn's disease and a method of treating osteoporosis.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
April 20, 2004

CEILA CHANG
PRIMARY EXAMINER
GROUP 1200 1625